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I would like to take the position that the FDA should not allow any medical claims be made on nutritional and nutraceutical products unless these pharmaceutical products have completed either registration under the traditional new drug application (NDC) or the homeopathic pharmacopoeia of the United States (HPUS). I am enclosing the following recently published articles in this arena. In brief my reasons are as follows:

A. Source of Raw Materials

It is well documented that there are both qualitative and quantitative differences of bioactive substances that are found in either botanical or biological sources of raw materials used for manufacture of these products.

B. Animal and Clinical Published Data

Studies that have been performed on botanical and biological products have been generally either poorly performed or do not represent the actual product that is added to the nutritional supplement.

C. Manufacturing Process

In general manufacturing of nutritional and nutraceutical products do not follow accepted guidelines for ethical pharmaceuticals. To ensure that rudimentary standards for all Nutraceutical Products the following requirements are mandatory and in compliance with the Current Good Manufacturing Practice and Quality Control Standards of the Food and Drug Administration.

Organization and Personnel

It is imperative that the quality control unit of the manufacturing process has the authority and responsibility for all of the functions that may affect quality of the finished product. This includes accepting or rejecting the individual product components, all product specifications, finished drug products, packaging and labeling.

Building and Equipment

Each building for the manufacture of nutraceutical products shall be of such structure, space, design and placement of equipment to enable thorough cleaning, inspection and safe and effective use for designated operations. Proper considerations must be given as to water quality, security, materials used for floors, walls and ceilings, segregated areas for raw materials subject to quality control approval (quarantine), weighing and measuring rooms, sterile areas for ophthalmic and parental products, flammable materials storage areas, finished product storage areas (quarantine),

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control of heat, humidity, light, temperature and ventilation, waste handling, employee facilities and safety procedures in compliance with the Occupational Safety and Health Administration (OSHA) regulation, procedures and practices.

Equipment

Each piece of equipment must be of appropriate design and size and suitably located to facilitate operations for its intended use, cleaning and maintenance. The equipment's surfaces and parts must not interact with the processes or product's components so as to alter the purity, strength or quality.

Control of Components

Written procedures are required to be maintained and followed describing the receipt, identification, storage, handling, sampling, testing and approval or rejection of the drug product components, containers or closures. All raw materials are quarantined until they are verified (qualitative, quantitative analysis, pyrogenicity and sterility) as meeting the required specifications.

Production and Process Controls

Written procedures are required for the production and process controls to assure that the drug products have the correct identity, strength, quality and purity. All materials and drug products must be withheld for use in packaging and labeling of the product until approved by the quality control unit. Labels must the label requirements and each expiration dating, production batch or lot number and NDC number if available.

Holding and Distribution

Written procedures must be established and followed for the holding and distribution of the finished product. Finished drug products must be quarantined in storage until released by the quality control unit.

Laboratory Controls

The establishment of and conformance to, written specifications and procedures, standards, sampling plans and/or other laboratory testing mechanisms must be developed and adhered to. They apply to each batch of drug product and must include sample size, testing intervals, sample storage, stability testing. Reserve samples must be retained for all drug products for specified time periods, usually for 3-6 months, following their expiration date. Reserve samples of the drug product used to conduct chemical analysis, bioavailablity and bioequivalence studies should be retained for 5 years.

Records and Reports

A complete master production and control record for each drug production batch should be maintained, including the name and strength of the product, dosage form, quantitative amounts of components and dosage units, complete manufacturing and control procedures, specifications, special notations, equipment used, in-process controls, sampling and laboratory methods used and assay results, calibration and instrumentation, distribution records and dated and employee identified records documenting that each step of the production, control, packaging, labeling and distribution of the drug product that was accomplished and approved by the quality control unit. All signatures must be verified (2). Any returned products must be identified by lot number, quality and quantity. These records must be available for inspection at any time. Computerized records that support all of the applications of drug product manufacture may provide the satisfactory requirements and authentication for good record keeping and reporting.

D. Scientific Methods for Verification of Components

Unfortunately, with complex mixtures of bioactive substances, there are no satisfactory, reproducible, universally acceptable or reliable methods for scientific verification/validation of each of the ingredients in these complex compounds. Moreover, the biological availiblity and biological action of these mixtures have not been scientifically determined. The available methods are as follows:

Infrared and Visible Spectroscopy

When organic molecules in solution are exposed to light in either the visible or ultraviolet spectrum they absorb light of particular and specific wave lengths depending upon the type of electronic transition that is associated with that absorption. The absorptivity depends not only on the molecule whose absorbance is being determined, but also on the type of solvent being used, as well as on the temperature and the wavelength of light employed for the analysis. Spectroscopy is a useful tool for studying the chemical equilibria or determining the rate of chemical reactions.

Mass Spectroscopy

The formation of charged species from a sample by collision with high-energy electrons or charges gaseous molecules is a partial vacuum is the fundamental process used in mass spectroscopy or mass spectrometry. These charged species may either be molecular ions or fragment ions from the sample. After formation, they are accelerated by a potential difference through an analyzer tube or collector. The analyzer tube can be placed between the poles of a magnet. The mass to charge ratio is thus equal to the magnetic field, the radius of curvature and the accelerating voltage.

Atomic Absorption Spectroscopy

Atomic spectra may be measured using bombardment of the sample with energy sources, such as gamma radiation. This technique is useful for individual qualitative and quantitative molecular analysis, but is of little value in the analysis of complexation and bonding.

Magnetic Resonance Spectroscopy

Magnetic resonance spectroscopy, previously called Nuclear Magnetic Resonance Spectroscopy, is a relatively new technology in which a magnetic wave is pulsed through the specimen and the characteristics of each component of the fluid that is measured as it absorbs the wave in differing degrees. A species with an odd number of electrons (unpaired) electrons placed in an external magnetic field will produce resonance between the energy levels of the unpaired electron's magnetic moment at a frequency in the microwave region of the electromagnetic spectrum. This resonance is associated with the spin of the unpaired electron, and the study of this effect is termed electron spin resonance or electron paramagnetic resonance.

E. Evaluation of bioactivity over the life spectrum of the product

Rarely, if ever, are any nutraceutical/nutritional product(s) evaluated for the possible new combinations or new potentially toxic bioactivity after the product has been manufactured and during the life expectancy of the product.

In conclusion: For any nutritional/nutraceutical drug product to make medical claims the FDA should require the same safety and efficacy standards as any pharmaceutical product making medical claims.

Sincerely,

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